Claims

1. Compounds of general formula I

$$\mathbb{A}$$
 \mathbb{A}
 \mathbb{A}

in which

X stands for CH or N,

W stands for hydrogen or fluorine,

A, B, D,

E and Q, in each case independently of one another, stand for a nitrogen or carbon atom, whereby only a maximum of two nitrogen atoms can be present in the ring,

R¹ stands for aryl or heteroaryl, which optionally can be substituted in one or more places in the same way or differently with halogen, hydroxy, C₁-C₁₂-alkyl, C₃-C₆-cycloalkyl, C₃-C₆-alkenyl, C₂-C₆-alkinyl, aralkyloxy, C₁-C₁₂-alkoxy, halo-C₁-C₆-alkyl, cyano-C₁-C₆-alkyl or with the group =O, -SO₂R⁶

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- or -OR⁵, whereby the C_1 - C_6 -alkyl optionally also can be substituted with the group -OR⁵ or -NR⁹R¹⁰,
- Y and Z, in each case independently of one another, stand for a bond or for the group =CO, =CS or = SO_2 ,
- $R^2 \ \text{and} \ R^3, \ \text{independently of one another, stand for hydrogen or for the group} \\ -CONR^9R^{10}, -SO^2R^6, -COR^{11}, -COC_1-C_6\text{-alkyl}, -CO-C_1-C_6\text{-alkyl-}R^{11}, \\ -NR^9R^{10} \ \text{or for} \ C_1-C_6\text{-alkyl}, \ C_3-C_{10}\text{-cycloalkyl}, \ C_3-C_6\text{-cycloalkenyl}, \ \text{aryl or heteroaryl that is optionally substituted in one or more places in the same} \\ \text{way or differently with halogen, cyano, } C_1-C_{12}\text{-alkyl}, \ C_1-C_{12}\text{-alkoxy}, \\ \text{hydroxy-}C_1-C_6\text{-alkyl}, \ \text{halo-}C_1-C_6\text{-alkyl} \ \text{or with the group} -NR^7R^8, \ -OR^5, \\ -C_1-C_6\text{-alkyl-}OR^5, \ -SR^4, \ -SOR^4 \ \text{or} \ -SO_2R^6, \ \text{or}$

 R^2 , R^3 , Y

- and Z together with the nitrogen atom form a 3- to 8-membered saturated or unsaturated ring, which optionally can contain additional heteroatoms in the ring and optionally can be substituted in one or more places in the same way or differently with halogen, cyano, C_1 - C_{12} -alkyl, C_1 - C_{12} -alkoxy, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, or with the group =O, -OR 5 , -SR 4 , -SOR 4 or -SO $_2$ R 6 ,
- R^4 stands for C_1 - C_{12} -alkyl, aryl or heteroaryl,
- stands for hydrogen, C_1 - C_{12} -alkyl, C_3 - C_{10} -cycloalkyl, C_1 - C_{12} -alkoxy, halo- C_1 - C_{12} -alkyl, or halo- C_3 - C_6 -cycloalkyl,
- R^6 stands for hydrogen, C_1 - C_{12} -alkyl, halo- C_1 - C_6 -alkyl, aryl or heteroaryl, or for the group -NR 9 R 10 , whereby the aryl or heteroaryl itself optionally can

be substituted in one or more places in the same way or differently with C_1 - C_1 -alkyl, C_1 - C_6 -alkoxy, halogen or halo- C_1 - C_6 -alkoxy,

 R^7 and R^8 , independently of one another, stand for hydrogen or $C_1\text{-}C_{12}\text{-}alkyl$,

R⁹ and R¹⁰, independently of one another, stand for hydrogen, C₁-C₆-alkyl,

 C_2 - C_6 -alkenyl, aryl, C_3 - C_8 -cycloalkyl or for the group $-CONR^7R^8$, or for C_1 - C_{12} -alkyl that is optionally substituted in one or more places in the same way or differently with aryl, morpholino, hydroxy, halogen, C_1 - C_{12} -alkoxy, or for the group $-NR^7R^8$, whereby the aryl itself optionally can be substituted in one or more places in the same way or differently with C_1 - C_6 -alkoxy or halo- C_1 - C_6 -alkyl, or

- R^9 and R^{10} together form a 5- to 8-membered ring that can contain additional heteroatoms, and
- R¹¹ stands for C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkoxy, C₃-C₆-cycloalkyl, phenyl, pyridyl, biphenyl or naphthyl, whereby the phenyl itself can be substituted in one or more places in the same way or differently with C₁-C₆-alkyl, or halo-C₁-C₆-alkyl, as well as isomers, diastereomers, tautomers and salts thereof.
- 2. Compounds of general formula I, according to claim 1, in which
- X stands for CH,
- W stands for hydrogen,

A, B, D,

E and Q as a ring together stand for pyridyl,

R¹ stands for aryl or heteroaryl, which optionally can be substituted in one or

more places in the same way or differently with halogen, hydroxy, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, C_4 - C_6 -alkenyl, C_2 - C_6 -alkinyl, aralkyloxy, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkyl, cyano- C_1 - C_6 -alkyl, or with the group =O, -SO₂R⁶ or -OR⁵, whereby C_1 - C_6 -alkyl optionally also can be substituted with the group -OR⁵ or -NR⁹R¹⁰,

Y and Z, in each case independently of one another, stand for a bond,

R² and R³, independently of one another, stand for hydrogen or for the group

-CONR⁹R¹⁰, -SO₂R⁶, -COR¹¹, -COC₁-C₆-alkyl, -CO-C₁-C₆-alkyl-R¹¹,

-NR⁹R¹⁰ or for C₁-C₆-alkyl, C₃-C₆-cycloalkyl, C₃-C₆-cycloalkenyl, aryl or heteroaryl that is optionally substituted in one or more places in the same way or differently with halogen, cyano, C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy-C₁-C₆-alkyl, halo-C₁-C₆-alkyl or with the group -NR⁷R⁸, -OR⁵,

-C₁-C₆-alkyl-OR⁵, -SR⁴, -SOR⁴ or -SO₂R⁶, or

 R^2 , R^3 , Y

- and Z together with the nitrogen atom form a 3- to 8-membered saturated or unsaturated ring, which optionally can contain additional heteroatoms in the ring and optionally can be substituted in one or more places in the same way or differently with halogen, cyano, C_1 - C_{12} -alkyl, C_1 - C_{12} -alkoxy, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl or with the group =0, -OR 5 , -SR 4 , -SOR 4 or -SO $_2$ R 6 ,
- R⁴ stands for C₁-C₆-alkyl, aryl or heteroaryl,
- R⁵ stands for hydrogen, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, C₁-C₁₂-alkoxy,
 C₃-C₁₀-cycloalkyl or halo-C₃-C₆-cycloalkyl,

stands for hydrogen, C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, aryl or heteroaryl, or for the group $-NR^9R^{10}$, whereby the aryl or heteroaryl itself optionally can be substituted in one or more places in the same way or differently with C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, halogen or halo- C_1 - C_6 -alkoxy,

 R^7 and R^8 , independently of one another, stand for hydrogen or C_1 - C_6 -alkyl,

- R^9 and R^{10} , independently of one another, stand for hydrogen, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, aryl, C_3 - C_8 -cycloalkyl, or for the group $-CONR^7R^8$, or for C_1 - C_6 -alkyl that is optionally substituted in one or more places in the same way or differently with aryl, morpholino, hydroxy, halogen or C_1 - C_{12} -alkoxy, or for the group $-NR^7R^8$, whereby the aryl itself optionally can be substituted in one or more places in the same way or differently with C_1 - C_6 -alkoxy or halo- C_1 - C_6 -alkyl, and
- R¹¹ stands for C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkoxy, C₃-C₆-cycloalkyl, phenyl, pyridyl, biphenyl or naphthyl, whereby the phenyl itself can be substituted in one or more places in the same way or differently with C₁-C₆-alkyl, or halo-C₁-C₆-alkyl, as well as isomers, diastereomers, tautomers and salts thereof.
- 3. Compounds of general formula I, according to claims 1 and 2, in which
- X stands for CH,
- W stands for hydrogen,

A, B, D,

E, and Q as a ring together stand for pyridyl,

R¹ stands for phenyl, quinolinyl, isoquinolinyl or indazolyl, which optionally

can be substituted in one or more places in the same way or differently with halogen, hydroxy, C_1 - C_6 -alkyl, C_2 - C_6 -alkinyl, C_1 - C_6 -alkoxy, halo- C_1 - C_6 -alkyl, or cyano- C_1 - C_6 -alkyl, whereby C_1 - C_6 -alkyl optionally also can be substituted with the group -OR⁵ or -NR⁹R¹⁰,

- Y and Z, in each case independently of one another, stand for a bond, or for the group =CO,
- R^2 and R^3 , independently of one another, stand for hydrogen or for the group $-CONR^9R^{10}, -SO_2R^6, -COR^{11}, -COC_1-C_6-alkyl, -CO-C_1-C_6-alkyl-R^{11}, \\ -NR^9R^{10} \ or \ for \ C_1-C_6-alkyl \ or \ phenyl \ that \ is \ optionally \ substituted \ in \ one \\ or \ more \ places \ in \ the \ same \ way \ or \ differently \ with \ the \ group \ -NR^7R^8 \ or \\ -OR^5, \ or$

 R^2 , R^3 , Y

- and Z together with the nitrogen atom form a 3- to 8-membered saturated or unsaturated ring that optionally can contain additional heteroatoms in the ring and optionally can be substituted in one or more places in the same way or differently with halogen, cyano, C_1 - C_{12} -alkyl, C_1 - C_{12} -alkoxy, halo- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl or with the group =O, -OR 5 , -SR 4 , -SOR 4 or -SO $_2$ R 6 ,
- R^5 stands for hydrogen or C_1 - C_6 -alkyl,
- R⁶ stands for hydrogen, C₁-C₆-alkyl, halo-C₁-C₆-alkyl, phenyl, benzyl, thiophenyl, or pyridyl, whereby the phenyl, benzyl, thiophenyl and pyridyl itself optionally can be substituted in one or more places in the same way

or differently with C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, halogen or halo- C_1 - C_6 -alkoxy,

 R^7 and R^8 , independently of one another, stand for hydrogen or C_1 - C_6 -alkyl, R^9 and R^{10} , independently of one another, stand for hydrogen, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, phenyl, biphenyl, C_3 - C_8 -cycloalkyl, naphthyl or for the group $-CONR^7R^8$ or for C_1 - C_6 -alkyl that is optionally substituted in one or more places in the same way or differently with phenyl, morpholino, hydroxy, halogen, C_1 - C_{12} -alkoxy, or with the group $-NR^7R^8$, whereby the phenyl itself optionally can be substituted in one or more places in the same way or differently with C_1 - C_6 -alkoxy or halo- C_1 - C_6 -alkyl, and

- stands for C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, hydroxy- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkoxy, C_3 - C_6 -cycloalkyl, phenyl, pyridyl, biphenyl or naphthyl, whereby the phenyl itself can be substituted in one or more places in the same way or differently with C_1 - C_6 -alkyl, or halo- C_1 - C_6 -alkyl, as well as isomers, diastereomers, tautomers and salts thereof.
- 4. Pharmaceutical agents comprise at least one compound of general formula I.
- 5. Pharmaceutical agents according to claim 4 for use in the case of tumor or metastasis growth, psoriasis, Kaposi's sarcoma, restenosis, such as, e.g., stent-induced restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia; arthritis, such as rheumatoid arthritis, hemangioma, angiofibroma; eye diseases, such as diabetic retinopathy, neovascular glaucoma; renal diseases, such as glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombic microangiopathic syndrome, transplant rejections and glomerulopathy; fibrotic diseases, such as cirrhosis of the liver, mesangial

cell proliferative diseases, arteriosclerosis, injuries to nerve tissue, inhibition of the reocclusion of vessels after balloon catheter treatment, vascular prosthetics or use of mechanical devices to keep vessels open, such as, e.g., stents, and as immunosuppressive agents, and for supporting scar-free healing, in senile keratosis and in contact dermatitis.

- 6. Pharmaceutical agents according to claim 5 for use as VEGFR kinase 3-inhibitors of lymphangiogenesis.
- 7. Compounds according to claims 1 to 3 and pharmaceutical agents, according to claims 4 to 6, with suitable formulations and vehicles.
- 8. Use of the compounds of formula I, according to claims 1 to 3, as inhibitors of the tyrosine kinases KDR and FLT.
- 9. Use of the compounds of general formula I, according to claims 1 to 3, in the form of a pharmaceutical preparation for enteral, parenteral and oral administration.
- 10. Use of the compounds according to claims 1 to 3 in the case of tumor or metastasis growth, psoriasis, Kaposi's sarcoma, restenosis, such as, e.g., stent-induced restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia; arthritis, such as rheumatoid arthritis, hemangioma, angiofibroma; eye diseases, such as diabetic retinopathy, neovascular glaucoma; renal diseases, such as glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombic microangiopathic syndrome, transplant rejections and glomerulopathy; fibrotic diseases, such as cirrhosis of the liver, mesangial cell proliferative diseases, arteriosclerosis, injuries to nerve tissue, and for inhibiting the reocclusion of vessels after balloon catheter treatment, in vascular prosthetics or after mechanical devices are used to keep vessels open, such as, e.g., stents, and as

immunosuppressive agents, and for supporting scar-free healing, and in senile keratosis and in contact dermatitis.

11. Compounds of general formulas II, IIa, and III,

$$(II),$$

$$W \cap R^{Y}$$

$$(III),$$

$$W \cap R^{Y}$$

$$V \cap R^{Y}$$

in which A, B, D, E, Q, W, X, Y, Z, R^2 , and R^3 have the meanings that are indicated in general formula I, and M stands for halogen, FG stands for a leaving group, such as, e.g., halogen, O-triflate, O-mesylate, O-tosylate or sulfone, and R^Y stands for C_1 – C_6 –alkyl or hydrogen, as intermediate products for the production of the compounds of general formula I according to the invention.